REMARKS

The Examiner is thanked for the courtesy of granting an interview, even though such interviews are discretionary for cases at the final rejection stage.

Applicants have carefully reviewed the Examiner's Office Action dated October 16, 2006, rejecting Claims 1 to 16 under 35 U.S.C. §103(a) as being unpatentable over WO 00/78292 (hereinafter the '292 Patent) in view of U.S. Patent No. 5,573,777 to Serpelloni, *et al.* (hereinafter "Serpelloni"). Additionally, the specification was objected to for allegedly failing to provide antecedent basis for the phrase "in amounts not preventing the tablet from disintegrating in the oral cavity within 60 seconds."

Via this amendment claims 1, 4, 8, and 13 have been amended. Claims 8 and 13 were amended to correct misspelling of the word "aspartame". Claims 1 and 4 were amended to specifically exclude cellulose. Support for this amendment is found in the object of the present invention, which is to ameliorate the disadvantages caused by the use of crystalline cellulose which may remain undissolved in the oral cavity to cause irritating sensation or poor organoleptic feel. This is described at page 2, lines 11 to 19 and page 3, line 4-16 of the present specification as filed. As shown, in comparative examples at page 12 of the present specification, using cross-linked carboxymethyl cellulose or low-substituted hydroxypropyl cellulose changes the hardness and disintegration time of the tablet as shown, for example, in Table 5.

Via this amendment, Applicants provide herein the basis for the phrase "in amounts not preventing the tablet from disintegrating in the oral cavity within 60 seconds" in the claims.

The phrase "rapidly disintegrating" refers usually to disintegration within 1 minute (60 seconds). This is a term of art. Support is found in the "Summary of the Invention" section of the specification at paragraph [0010] which states, "In accordance with the present invention, there is provided a tablet for oral administration, which disintegrates in the oral cavity within 60 seconds...." Applicants further direct the Examiner to Tables 4, 5, 6, and 8 of the specification of the present invention, where for each of examples 1-13 as shown in Tables 4-6 and Test Example 6 as shown in Table 8, the disintegration time falls between a range of 20.7 to 55 seconds. A disintegration time of 55 seconds is encompassed by the phrase "less than 60 seconds."

Applicants traverse the 35 U.S.C. §103(a) rejection. In view of the above amendments made to the claims and for the reasons provided below, early allowance of the pending claims is respectfully requested.

Via this amendment Applicants submit a §132 Inventor Affidavit to show the product of the present invention differs from that of the references cited. Since the only remaining rejection is under 35 U.S.C. §103, Applicants submit that this experimental data or arguments or references which distinguish the present invention to show unexpected results and the advantages of the product thus produced should overcome the rejection. This experimental data shows the unexpected nature of the process and the formulation over the '292 tablet using the mannitol of Serpelloni. Table 1 of the Inventor affidavit shows that the addition of cellulose as in tablets B to D increases the disintegration time. Even combining the spray dried mannitol of Serpelloni into the tablet of the '292 Patent does not result in the disintegration time of less than 60 seconds as in the present invention.

Inasmuch as Serpelloni relates to a pulverulent mannitol, it also fails to teach, suggest, or imply "no use of cellulose compound" according to the present invention. The '292 Patent requires cellulose as an essential element whereas, as amended, Claims 1 and 4 of the present invention specifically exclude cellulose.

With regard to spray-dried mannitol, which the '292 Patent does not disclose, the Examiner maintains that Serpelloni teaches this feature. According to the Examiner, it would have been obvious to one skilled in the art to modify the '292 Patent with the mannitol of Serpelloni inasmuch as the product would be suitable for those who have difficulty swallowing oral medications.

Applicants respectfully disagree and maintain that thee is no motivation to combine the '292 Patent and Serpelloni.

Serpelloni is directed to a mannitol with a particular friability, density and particle size and production of same for the purpose of improved friability and dissolution. There is no mention in Serpelloni of use in solid dosage forms which disintegrate in the oral cavity. There is a vast difference between dissolution which involves standard testing procedures (e.g. United States Pharmacopeia) such as stirring speeds and disintegration in the oral cavity via saliva. The attached article by Narazaki, R, et al., A New Method for Disintegration Studies of Rapid Disintegrating Tablet, *Chem. Pharm. Bull.* 52:704-707 (2004), at column 1, paragraph 3 states, "At present, the disintegration time of RDT's is measured utilizing the conventional tests (for tablets) that are described in the Pharmacopoeias. However, it is difficult to assess the disintegration rate for the RDT with these tests due to its rapid disintegration rate even in a small

amount of water. Further the conventional tests employ a volume of 900 ml of test solution compared to the volume of saliva in humans, which is less than 1 ml. Thus, the disintegration rate obtained from the conventional disintegration tests appears not to be reflective of the disintegration rate in the human mouth." The formulations of present invention result in disintegration in the oral cavity within 60 seconds whereas in Serpelloni, the dissolution time profile involves stirring at 200 rpm in a beaker of 150 grams of water. In fact, as described in the specification, spray dried mannitol has a dissolution of about 5 seconds. Oral disintegration of a specific combination of pharmaceutical agent, spray-dried mannitol and crospovidone and dissolution testing of a mannitol that undergoes **BOTH** atomization and granulation are not correlatable.

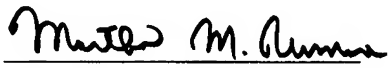
There is no suggestion whatsoever in Serpelloni for use of mannitol in quick dissolving dosage forms, let alone oral cavity quick dissolving dosage forms which dissolve in less than 60 seconds. Nor is there any suggestion to include the mannitol of Serpelloni with co-processed crospovidone in direct compression. Further, the present invention is directed to spray-dried mannitol combined with the hygroscopic disintegrant crospovidone. There is no suggestion or teaching in Serpelloni for such combination.

Accordingly, Applicants respectfully submit that there is nothing *prima facie* obvious about the present invention. Moreover, the references cited by the Examiner are not the least persuasive that one of ordinary skill in the art would find the present invention obvious over these references.

In view of the foregoing amendments and discussions, it is respectfully submitted that the present invention as defined in the pending claims 1 to 16 is in full compliance with all the statutory requirements, and therefore, it is earnestly requested that the Examiner's rejections be withdrawn and the pending claims be allowed in their present form.

Any fee due with this paper, not fully covered by an enclosed check, may be charged on Deposit Account 50-1290.

Respectfully submitted,



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